The heart in systemic lupus erythematosus

A cause of myocardial infarction in a man of 20

History
March 1982—An 18 year old man presented with a three week history of abdominal distension and swelling of the face and ankles. He had not done a history of risk factors for ischaemic heart disease. He was febrile (38°C), and the physical findings were of massive leg and sacral oedema, ascites, and a left sided pleural effusion. Table I gives details of the investigations. A chest radiograph showed a left sided pleural effusion. Renal biopsy specimens showed mesangiocapillary glomerulonephritis, and skin biopsy specimens showed deposition of IgG and complement at the dermoepidermal junction. After immunosuppressive treatment was started his serum albumin concentration increased to 28 g/l and the DNA binding fell to 30%.

December 1982—He presented with acute pleuritic pain in association with a deep venous thrombosis of his right leg. A ventilation-perfusion lung scan showed mismatch strongly suggestive of pulmonary embolism, and he was treated with warfarin. He had a further episode of pleuritic pain six months later.

July 1984—He presented with a five day history of increasing central chest pain. An electrocardiogram showed an acute inferior myocardial infarction. Other investigations showed a creatinine concentration of 95 mmol/l and a 24 hour urine protein measurement of 11·9 g. Lupus anticoagulant and anticardiolipin antibodies were present. A coronary angiogram showed normal coronary arteries, but an echocardiogram showed inferior akinesia. His fasting cholesterol concentration was 8·0 mmol/l. Immunosuppressive treatment was continued with azathioprine and prednisolone. He made an uneventful recovery and was free of symptoms with unlimited effort tolerance for the next four years.

August 1988—He presented with a history of central
chest pain, and an electrocardiogram taken on admission showed an acute anterolateral myocardial infarction. His blood pressure was 120/95 mm Hg.

January 1989—He was referred back to this hospital with signs of congestive cardiac failure. Investigations showed an erythrocyte sedimentation rate of 27 mm in the first hour, blood urea concentration of 6-8 mmol/l, creatinine concentration of 89 μmol/l, and creatinine clearance of 1-42 ml/s. Lupus anticoagulant and anticardiolipin antibodies (IgG 39 U/l (normal <9 U/l) and IgM 1-8 U/l (normal <8 U/l)) were present. Table II gives the data from cardiac catheterisation. Coronary angiography showed extensive triple vessel disease (fig 1).

**Discussion**

Figure 2 shows a summary of the interactions in systemic lupus erythematosus and coronary heart disease.

CMO: We do not know why some patients with active systemic lupus erythematosus develop valvular heart disease while others develop coronary thrombosis. This young man had near normal coronary arteries at presentation and now has appearances that are indistinguishable from those of severe atheroma, though I have little doubt that these lesions were initiated by arteritis and postarteritic thrombotic events.

MJW: The role of antiphospholipid antibodies in the pathogenesis of cardiac lesions is of great interest. We have previously presented on the staff round a patient with severe aortic regurgitation who had anticardiolipin antibodies but did not have any other clinical features or autoantibodies to allow the diagnosis of systemic lupus erythematosus. Such patients have been labelled as suffering from the "primary antiphospholipid syndrome." The prevalence of clinically important cardiac valvular lesions in these patients has been estimated to be as high as 18%. Several reports have associated these lesions with the presence of antiphospholipid antibodies. Whether there is a causal link between antiphospholipid antibodies and valvular damage has not been established. Antiphospholipid antibodies from patients with systemic lupus erythematosus and the primary antiphospholipid syndrome bind predominantly to negatively charged phospholipids, which are ubiquitous on the inner lamella of cell membranes. Whether negatively charged phospholipids are available in vivo for the extracellular binding of these antibodies is uncertain, and no convincing evidence has been presented for such binding. Possibly anticardiolipin antibodies are acting as a marker for another, unidentified, autoantibody that is relevant to the cause of the disease.

The relation of anticardiolipin antibodies to coronary thrombosis is intriguing. There is a raised incidence of myocardial infarction among patients with systemic lupus erythematosus and this is an important cause of death. It has been attributed to accelerated atherosclerosis in coronary arteries damaged by vasculitis and hyperlipidaemia. The MRL/lpr mouse is an experimental model of systemic lupus erythematosus in which such a train of events seems to occur, though extrapolation from mice to humans is a dubious exercise. High density lipoprotein cholesterol is reduced in patients with active systemic lupus erythematosus, and long term treatment with steroids is associated with raised low density lipoprotein cholesterol and triglyceride concentrations. The changes in

**TABLE II—Data from cardiac catheterisation**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Value</th>
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<tbody>
<tr>
<td>Pressure (mm Hg):</td>
<td></td>
</tr>
<tr>
<td>Right atrium</td>
<td>8</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>50/16</td>
</tr>
<tr>
<td>Main pulmonary artery</td>
<td>50/30</td>
</tr>
<tr>
<td>Pulmonary artery (mean)</td>
<td>80</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>125/30</td>
</tr>
<tr>
<td>Aorta</td>
<td>120/95</td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td>4-77</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>2-51</td>
</tr>
</tbody>
</table>
lips resulting from the nephrotic syndrome may have been an additional risk factor in this patient.

The possible links between antcardiolipin antibody and myocardial infarction in patients without overt autoimmune disease are controversial. Raised titres of these antibodies have been reported in consecutively ascertained patients with myocardial infarction and in patients with myocardial ischaemia. In the study of Blasen et al, however, the incidence of myocardial infarction was low compared with that measured in patients with systemic lupus erythematous, and whether the antibody or the atheroclesis came first has not been established.

PN: We have studied 54 consecutive patients with this condition by two dimensional echocardiography with the aim of identifying factors of importance in the pathogenesis of associated cardiac disease. The abnormalities identified were predominantly of two types: valvular vegetations (principally affecting the mitral valve) and myocardial dysfunction. Patients with raised antcardiolipin antibody titres had a higher incidence of cardiac disease. These were absent in only one patient with systemic lupus erythematous and Libman-Sacks vegetations on the mitral valve. We have also screened 40 patients with antcardiolipin antibodies but without evidence of systemic lupus erythematous and found that patients with antcardiolipin antibodies had a high incidence of cardiac abnormalities. Thus, cardiac disease suggested by these abnormalities on two dimensional echocardiography is highly correlated with the presence of high titres of antcardiolipin antibodies without other features of systemic lupus erythematous.

SRB: The patient had considerable lipid abnormalities. Could you suggest the importance of these in the development of his accelerated coronary artery disease?

GRT: Possibly the sequence of events was as follows. The thrombotic tendency associated with systemic lupus erythematous was almost certainly responsible for the patient's first myocardial infarct, when his angiogram was normal. The hyperlipidaemia that accompanied his nephrotic syndrome during 1984-8, however, must have been a major additional factor in the development of the triple vessel disease that culminated in his second myocardial infarct. If this patient were presenting today the drug of first choice to treat the hyperlipidaemia would be a hydroxy-3-methylglutaryl coenzyme A reductase inhibitor such as lovastatin. Our experience and that of others is that such drugs are highly effective in reducing low density lipoprotein cholesterol concentrations in the nephrotic syndrome.

SRB: The patient has triple vessel disease and a poorly functioning myocardium. Is cardiac transplantation an option?

CMO: His cardiac failure is at present well controlled by an angiotensin converting enzyme inhibitor and diuretic treatment. Transplantation is, however, an important treatment option here and needs to be considered seriously despite anxiety about recurrence of the primary disease in the transplanted organ, I think, to the risk of recurrent vasculitis.

AJR: How is the successful use of cardiac transplantation in patients with systemic lupus erythematous shows that recurrence does occur but that the incidence is rather low. It would therefore seem entirely reasonable to consider cardiac transplantation in this patient.


ANY QUESTIONS

Is there a place for corticosteroid administered by depot injections in the treatment of hay fever?

When administered prophylactically corticosteroids are effective in controlling the symptoms of hay fever. For this purpose they may be administered by inhalation, orally, or as intramuscular depot injections. For the symptoms of sneezing, rhinorrhoea, and conjunctivitis the selective H1 antagonists, such as terfenadine, astemizole, and citizirine, are the drugs of choice as these symptoms are mainly caused by allergen triggered release of histamine from the increased number of mast cells that colonise these mucosal surfaces in sensitised subjects during the pollen season. When severe symptoms are expected treatment should be started before the onset of the pollen season. With increasing symptoms, especially when they include nasal blockage, corticosteroids are indicated. The prophylactic use of topical corticosteroids in the form of aqueous aerosol or pressurised metered dose aerosols (beclomethasone dipropionate, flunisolide) provides good protection for most people. Ideally these should be started regularly, either before the pollen season or when symptoms first appear, and continued throughout the season. Their mechanism(s) of action include the reduction or prevention of mast cell hyperplasia stimulated by the allergen, reduction in basophil and eosinophil infiltration, and their well known antiedema effect.1 When administered twice daily in the recommended dose this route of administration of corticosteroid has no effect on the pituitary-adrenal axis. Depot corticosteroid injections, such as betamethasone dipropionate and methylprednisolone acetate, are also effective in ameliorating the symptoms of hay fever. To achieve their effects a persistent increase in the plasma concentration of corticosteroid is required and persists for about four weeks. A single injection of depot corticosteroid is approximately equivalent to 7-5 mg of prednisolone daily for three to four weeks. Adrenal suppression is almost certainly associated with depot corticosteroid injections. This also lasts for about four weeks after a single intramuscular injection and up to 12 weeks with two treatments. For this reason patients who have received this form of treatment should carry a "steroid card." Other potential hazards of systemic corticosteroids on electrolyte balance, bone metabolism, and growth are additional reasons for avoiding this form of treatment for hay fever whenever possible.

Their use may be advocated when a combination of inhaled cortico
dosterone and H1 antagonists fail to control symptoms2 and when symptoms will coincide with an important life event—for example, examinations, marriage. Thus, though depot corticosteroid preparations are considerably less expensive and more convenient than the regular use of antihistamines and topical corticosteroids, concern over their systemic side effects is the main reason why their use has fallen out of favour. — S T HOLGATE, clinical professor of immunopharmacology, Southampton